Scottish Paediatric Endocrine Group (SPEG)

Hypoglycaemia Guideline

NOTE
This guideline is not intended to be construed or to serve as a standard of care. Standards of care are determined based on all clinical data available for an individual case and are subject to change as scientific knowledge and technology advance and patterns of care evolve. Adherence to guideline recommendations will not ensure a successful outcome in every case, nor should they be construed as including all proper methods of care or excluding other acceptable methods of care aimed at the same results. The ultimate judgement must be made by the appropriate healthcare professional(s) responsible for clinical decisions regarding a particular clinical procedure or treatment plan. This judgement should only be arrived at following discussion of the options with the patient, covering the diagnostic and treatment choices available. It is advised, however, that significant departures from the national guideline or any local guidelines derived from it should be fully documented in the patient's case notes at the time the relevant decision is taken.

Blood glucose in children is normally within a range 3.5 and 6.0 mmol/L. Hypoglycaemia is usually defined as a blood glucose level of <2.6 mmol/L. Of note, low glucose can be normal in infants up to 72hr of age. The maintenance of a normal blood glucose level is a complex process involving carbohydrate intake and absorption, gluconeogenesis and glycogenolysis.

Signs & symptoms

Signs and symptoms of hypoglycaemia can vary greatly between individuals. Early features are associated with adrenergic responses including pallor and sweating. As hypoglycaemia persists, neurological symptoms occur due to impaired glucose supply to the brain.

Severity	Symptoms	Signs
Mild	Sweating Headache Anxiety	Tachypnoea tremor Pallor Lethargy
Moderate	Jitteriness Nausea & vomiting	Changes in behavior Slurred speech Unsteady gait
Severe	Dizziness Visual disturbances	Altered consciousness Convulsions

The predominance and severity of symptoms depends on the age of the patient, the rapidity of onset and duration of the hypoglycaemia.

The investigation and treatment of symptomatic hypoglycaemia is a medical emergency as delayed treatment can have severe consequences including permanent brain damage.

Cause	Condition
Systemic/Nutritional	Starvation Malnutrition Sepsis Malabsorption
Metabolic	Fatty acid oxidation defects Organic acidopathies Disorders of carbohydrate metabolism Disorders of gluconeogenesis
Endocrine	Hyperinsulinism Adrenal insufficiency Hypopituitarism Hypothyroidism Growth hormone deficiency
Toxic	Aspirin Alcohol Insulin Valporate
Hepatic	Hepatitis Cirrhosis Reye syndrome

Idiopathic ketotic hypoglycaemia is the most common cause of hypoglycaemia in children after the neonatal period. This is usually precipitated by a relatively mild illness.

Patient history

A good clinical history is essential as it may help direct initial investigations.

GENERAL

- age at presentation
- presenting features
- inter-current illness
- length of fasting
- history of drug or alcohol use e.g. inhaled steroids

PAST HISTORY

- previous similar episodes (may be unrecognised e.g. seizures)
- neonatal hypoglycaemia
- family history of unexplained infant death

CLINICAL FEATURES

- hepatomegaly
- neonatal hypoglycaemia
- hyperpigmentation
- short stature

Investigation of Hypoglycaemia

Documentation of the circumstances of hypoglycaemia screen can be very helpful in interpretation (e.g. timing of sampling compared to glucose being given).

TIME CRITICAL SAMPLES: Collect PRIOR to administration of glucose.
**Tests are listed in order of priority **

Test	Tube Type (minimum volume)
Glucose Free fatty acids (NEFA) Lactate	Fluoride oxalate (1ml)
Cortisol B-hydroxybutyrate Insulin* / C-peptide*	Lithium heparin (1.5ml) ***Note: Tube types – suggest contact local laboratory***

* Labile samples – must reach laboratory as soon as possible (ideally within 30 minutes of collection). ***Save any residual sample for possible further tests if indicated.***

ADDITIONAL ESSENTIAL SAMPLES: Collect AFTER administration of glucose.
**Tests are listed in order of priority **

Test	Tube Type (minimum volume)
Urea & Electrolytes Liver function tests CRP Thyroid function tests	Lithium heparin (1.5ml)
Ammonia Plasma amino acids $Acylcarnitine	Lithium heparin (1.5ml) $Bloodspot (x 2-3) or plasma
Full blood count	EDTA (1ml)
Urine organic acids	Plain universal container, no preservatives (5-10ml)

Save any residual sample for possible further tests if indicated.

Interpretation

GENERAL BIOCHEMISTRY

General biochemistry may give you some clues into the cause of hypoglycaemia. For example:

- Hyponatraemia with hyperkalaemia: Suggestive of endocrine disorder of adrenal or pituitary origin
- abnormal liver function tests: present in a number of metabolic disorders e.g. glycogen storage disorders. Also indicative of any cause of liver dysfunction.
- elevated lactate: present in a number of metabolic disorders e.g. defect of energy metabolism or glycogen storage disorders.
- Hyperammonaemia: associated with many organic acidopathies

INTERMEDIATE METABOLITES

Samples must be taken at time of hypoglycaemia to allow accurate interpretation.

- low β-hydroxybutyrate and NEFA - Suggestive of hyperinsulinism
- NEFA ratio/ β-hydroxybutyrate ≤ 1- Appropriate lipolytic and ketogenic response to hypoglycaemia
- NEFA ratio/ β-hydroxybutyrate ³1- Suggestive of fatty acid oxidation defect, ketogenic disorder or carnitine deficiency.

ENDOCRINE TESTS

- detectable Insulin – If sample taken during hypoglycaemia indicates hyperinsulinism
- low cortisol – Indicates either hypoadrenalism or hypopituitarism

AMINO ACIDS

- raised branch chain (ketogenic) and gluconeogenic amino acids are seen in ketotic hypoglycaemia

ACYLCARNITINES

- specific acylcarnitine species will be raised if there is a fatty acid oxidation defect or organic acidaemia

ORGANIC ACIDS

- ketone bodies and dicarboxylic acids are seen as a part of the normal response to hypoglycaemia
- specific organic acids e.g. glycines, will usually be present in a crisis sample from patients with fatty acid oxidation defects or organic acidaemias
- elevated lactate can been seen in patients with glycogen storage disorders, defects of gluconeogenesis, organic acidaemias and congenital lactic acidaemias

URINE CHEMISTRY

- urine ketones are often negative or inappropriately low in fatty acid oxidation defects.